REMARKS

Status of the Claims

Claims 1-10 are pending. Claims 11-20 have been canceled. Claim 1 has been amended in order to present consistent terminology for the "one or more drugs" without changing the scope of the claim regarding this point. Claim 1 has also been amended to recite the amount of surfactant as will be discussed further below.

Support for the amendment to claim 1 regarding the amount of the surfactant can be found throughout the specification, including page 6, lines 9-17 and in the Examples.

Specification

The Examiner has objected to the abstract because it is not a complete sentence. The abstract has been amended to overcome the objection and also in order to more accurately reflect what is disclosed in the specification.

Double Patenting Rejection

Claims 11-20 of the present application are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over (1) claims 1-5 of U.S. Patent No. 6,743,413 in view of Purewal et al., U.S. Patent No. 5,225,183; (2) claims 1-11 of U.S. Patent 5,427,282; and (3) claim 19 of U.S. Patent 6,054,488. In order to advance prosecution, and without conceding the propriety of these rejections, claims 11-20 have been canceled

without prejudice to or disclaimer of the subject matter contained therein. Applicants reserve the right to pursue these claims in a continuation application.

Rejection Under 35 U.S.C. § 102

Claims 1-20 are rejected under 35 U.S.C. § 102(e) as being anticipated by Byron et al., U.S. Patent No. 5,182,097. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are respectfully requested.

In explaining his rejection, the Examiner has referred in particular to Col. 2, lines 47-50 and 56-60 and Col. 5, line 58 to Col. 6, line 6 of Byron et al. However, in order to fully understand the teaching of Byron et al., additional disclosure in Byron et al. must also be considered, as explained below.

Byron et al. discloses that an object of the invention is to provide MDI formulations that "include a drug and a surfactant" (Col. 2, lines 57-58). Byron et al. uniformly discloses formulations that include a surfactant. See, for example, Col. 2, line 64 to Col. 3, line 12, which reads in pertinent part,

> According to the invention, experiments were conducted to reformulate a typical MDI product to reduce or eliminate the use of chlorofluorocarbons. In the experiments, micronized albuterol was used as the drug product and oleic acid was used as the surfactant, although those skilled in the art will recognize that the medicaments may be chosen and varied to suit the objective of drug deliver[ed] to the lungs of the patient. The ideal alternative propellant will satisfy the following criteria. (1) The propellant blend should consist of a single liquid phase a room temperature, (2) the surfactant (oleic acid) should dissolve in the propellant blend, (3) the micronized drug (albuterol) should be easily dispersible in the propellant blend with the aid of the surfactant (oleic acid)... (emphasis added)

All test formulations of Byron et al. contain surfactant (Col. 4, lines 39-42, "Each test formulation was prepared by adding...micronized albuterol and...oleic acid...") and all working examples require surfactant (Col. 2, lines 66-68, "In the experiments, micronized albuterol was used as the drug product and oleic acid was used as the surfactant...").

Byron's consistent disclosure of the inclusion of significant amounts of surfactant plainly indicates to one skilled in the art that Byron et al. considered surfactant to be a necessary ingredient of the aerosol formulations. Although Byron et al. discusses the possibility of varying the amount of drug and surfactant in order to achieve inhalation drug delivery (see, for example, Col. 3, lines 1-4), surfactant is necessary in an amount to stabilize the formulation to form a suitable dispersion. Byron et al. does not contemplate preparing a metered dose inhaler using a formulation that contains no surfactant or that contains only very small (non-stabilizing) amounts of surfactant.

Indeed, Byron et al. actually directs the skilled artisan to consider other commercially known surfactants when oleic acid is not suitable. For example, Byron et al. states, "the micronized drug (albuterol) should be easily dispersible in the propellant with the aid of the surfactant (oleic acid)" (see, Col. 3, lines 8-11, emphasis added), and if oleic acid fails to dissolve, "other surfactants utilized in commercial MDIs (e.g., sorbitan trioleate and soya lecithin), are known to exhibit different solubility characteristics and may be suitable for use with propellant blends in which oleic acid failed to dissolve" (see, Col. 6, lines 23-27).

In contrast, according to present claim 1 (as amended herein), a "pharmaceutical suspension formulation [which] contains no surfactant or less than an effective stabilizing

amount of surfactant" is used to prepare a metered dose inhaler. Such language serves to either exclude the surfactant altogether or indicate that the surfactant is present in less than a stabilizing amount. Accordingly, there can be no anticipation based upon the disclosure of Byron et al. This rejection should therefore be withdrawn.

Additionally, it is submitted that there should also be no obviousness based upon the Byron et al. reference either by itself or combined with other prior art of record. The currently pending claims have been amended to indicate that the pharmaceutical suspension formulation used to prepare the metered dose inhaler "contains no surfactant or less than an effective stabilizing amount of surfactant." This either excludes the surfactant altogether or indicates that the surfactant is present in less than a stabilizing amount. However, such a limitation is directly contrary to the teachings of Byron et al. and is compelling evidence of the both (1) the lack of anticipation as discussed above, and (2) non-obviousness of the present invention. "A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." U.S. Pat. & Trademark Off., Manual Pat. Examining Proc. § 2141.02 (8th ed. Rev. 1, Feb. 2003); W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

To further illustrate the above, it is noted that Byron co-authored an article which explicitly sets forth his view that surfactant was a required component of an aerosol formulation for a metered dose inhaler (MDI). Byron, Dalby et al., "CFC Propellant Substitution: P-134a as a Potential Replacement for P-12 in MDIs" Pharmaceutical Technology, March 1990. According to the article, one of the critical tests to be passed by any replacement propellant is its ability to

dissolve the surfactants used in such formulations. See, page 4, lines 9-10. This test is repeated by Byron et al. in the '097 patent at Col. 3, lines 7-8, "[T]he surfactant (oleic acid) should dissolve in the propellant blend...." Given that Byron believed surfactant was a crucial component of an aerosol formulation, Applicants' use of pharmaceutical suspension formulations containing no surfactant, or less than a stabilizing amount of a surfactant, is non-obvious. "The totality of the prior art must be considered, and proceeding contrary to accepted wisdom in the art is evidence of nonobviousness." U.S. Pat. & Trademark Off., Manual Pat. Examining Proc. § 2145 (8th ed. Rev. 1, Feb. 2003); In re Hedges, 783 F.2d 1038 (Fed. Cir. 1986).

Accordingly, there can be neither anticipation nor obviousness of the present claims based upon Byron et al. Reconsideration and withdrawal of the rejection for these reasons is respectfully requested.

Rejection Under 35 U.S.C. § 103

Claims 1-20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Purewal et al., U.S. Patent No. 5,225,183 by itself or in view of Byron. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are respectfully requested.

The Examiner appears to recognize that Purewal teaches that a surfactant is an important ingredient (see the paragraph bridging pages 7 and 8 of the Office Action) of an aerosol formulation. For the reasons discussed above, and particularly in view of the amended claims, it is respectfully submitted that Byron et al. does not cure the deficiencies of Purewal. Neither Purewal nor Byron, whether taken individually or in combination, suggest or disclose a pharmaceutical

suspension formulation that "contains no surfactant or less than an effective stabilizing amount of surfactant." Therefore, it would not be obvious to use such formulations to prepare a metered dose inhaler as claimed.

For the foregoing reasons, it is respectfully submitted that the claims are patentable over the cited references.

Miscellaneous Comments

The Examiner should note that in parent Application No. 08/455,280 (now U.S. Patent 6,743,413 B1, Primary Examiner Thurman Page), certain arguments were made to distinguish the claims therein over Byron et al., U.S. Patent 5,190,029. The Byron et al. patent cited by the Examiner in the present application (U.S. 5,182,097, which was also of record in the parent application) issued from the parent of the '029 patent, and thus has the same disclosure. The Purewal patent cited by the Examiner (U. S. Patent 5,225,183) was also of record in the parent application.

Information Disclosure Statement

The Examiner's attention is directed to the Information Disclosure Statement filed concurrently herewith. It is submitted that the claims in this application are patentable over the additional references cited in the Information Disclosure Statement.

Conclusion

If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to contact the undersigned at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

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